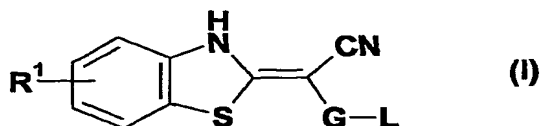


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Claims

1. Use of benzothiazole derivatives according to formula I



- 5 as well as its tautomers, its geometrical isomers, its optically active forms as enantiomers, diastereomers and its racemate forms, as well as pharmaceutically acceptable salts thereof, wherein

G is an pyrimidinyl group.

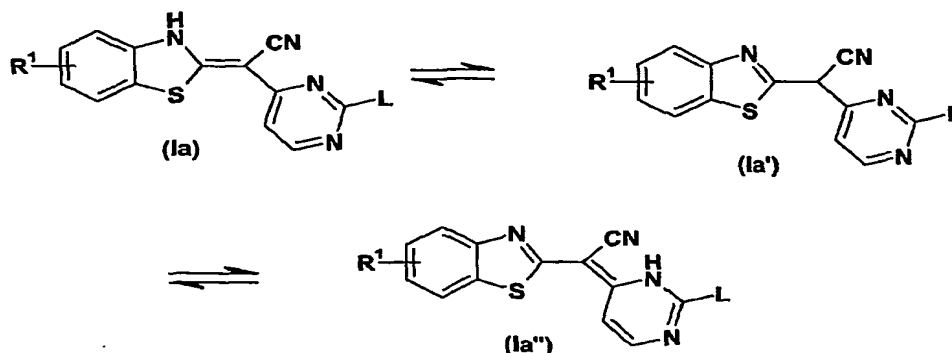
- 10 L is an C₁-C₆-alkoxy, or an amino group, or an 3-8 membered heterocycloalkyl, containing at least one heteroatom selected from N, O, S;

R¹ is selected from the group comprising or consisting of hydrogen, sulfonyl, amino, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl or C₁-C₆-alkoxy, aryl, halogen, cyano or hydroxy.

- 15 for the preparation of a medicament for the treatment of metabolic disorders mediated by insulin resistance or hyperglycemia, comprising diabetes type II, inadequate glucose tolerance, insulin resistance, obesity, polycystic ovary syndrome (PCOS).

2. Use according to claim 1, wherein the disease is diabetes type II.
3. Use according to claim 1 or 2, wherein R¹ is H or C₁-C₃ alkyl.
4. Use according to any of claims 1 to 3, wherein the compound has any of formulae (Ia),
20 (Ia') or (Ia'') :

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wherein R^1 is selected from the group comprising or consisting of hydrogen, sulfonyl, amino, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl or C_1 - C_6 -alkoxy, aryl, halogen, cyano or hydroxy. and

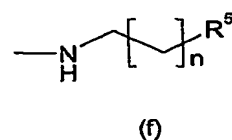
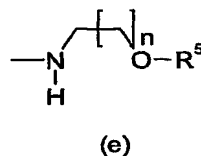
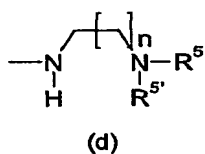
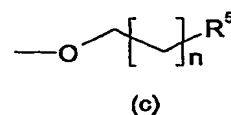
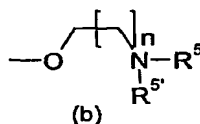
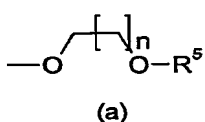
- 5 L is an amino group of the formula $-NR^3R^4$ wherein R^3 and R^4 are each independently from each other H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, C_1 - C_6 -alkoxy, aryl, heteroaryl, saturated or unsaturated 3-8-membered cycloalkyl, 3-8-membered heterocycloalkyl, (wherein said cycloalkyl, heterocycloalkyl, aryl or heteroaryl groups may be fused with 1-2 further cycloalkyl, heterocycloalkyl, aryl or heteroaryl group), C_1 - C_6 -alkyl aryl, C_1 - C_6 -alkyl heteroaryl, C_1 - C_6 -alkenyl aryl, C_1 - C_6 -alkenyl heteroaryl, C_1 - C_6 -alkynyl aryl, C_1 - C_6 -alkynyl heteroaryl, C_1 - C_6 -alkyl cycloalkyl, C_1 - C_6 -alkyl heterocycloalkyl, C_1 - C_6 -alkenyl cycloalkyl, C_1 - C_6 -alkenyl heterocycloalkyl, C_1 - C_6 -alkynyl cycloalkyl, C_1 - C_6 -alkynyl heterocycloalkyl, or
- 10 R^3 and R^4 may form a ring together with the nitrogen to which they are bound.

- 15 5. Use according to claim 4, wherein R^3 is hydrogen or a methyl or ethyl or propyl group and R^4 is selected from the group consisting of (C_1 - C_6)-alkyl, C_1 - C_6 alkyl-aryl, C_1 - C_6 -alkyl-heteroaryl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl and 4-8 membered saturated or unsaturated cycloalkyl.
- 20 6. Use according to claim 4, wherein R^3 and R^4 form an optionally substituted piperazine or a piperidine or a morpholine or a pyrrolidine ring together with the

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nitrogen to which they are bound, whereby said optional substituent is selected from the group consisting of C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, aryl, heteroaryl, saturated or unsaturated 3-8-membered cycloalkyl, 3-8-membered heterocycloalkyl, (wherein said cycloalkyl, heterocycloalkyl, aryl or heteroaryl groups may be fused with 1-2 further cycloalkyl, heterocycloalkyl, aryl or heteroaryl group), C₁-C₆-alkyl aryl, C₁-C₆-alkyl heteroaryl, C₁-C₆-alkenyl aryl, C₁-C₆-alkenyl heteroaryl, C₁-C₆-alkynyl aryl, C₁-C₆-alkynyl heteroaryl, C₁-C₆-alkyl cycloalkyl, C₁-C₆-alkyl heterocycloalkyl, C₁-C₆-alkenyl cycloalkyl, C₁-C₆-alkenyl heterocycloalkyl, C₁-C₆-alkynyl cycloalkyl, C₁-C₆-alkynyl heterocycloalkyl.

10 7. Use according to claim 5 wherein L is selected from :



wherein n is 1 to 10, preferably 1 to 6,

R⁵ and R^{5'} are independently selected from each other from the group consisting of H, C₁-C₁₀ alkyl, aryl or hetero-aryl, C₁-C₆ alkyl-aryl and C₁-C₆-alkyl-heteroaryl.

15 8. Use according to any of the preceding claims wherein the compound is selected from the following group:

1,3-benzothiazol-2-yl(2,6-dimethoxy-4-pyrimidinyl)acetonitrile

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- 1,3-benzothiazol-2-yl(2-{[2-(1H-imidazol-5-yl)ethyl]amino}-4-pyrimidinyl)acetonitrile
- 1,3-benzothiazol-2-yl[2-(1-piperazinyl)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl[2-(4-benzyl-1-piperidinyl)-4-pyrimidinyl]acetonitrile
- 5 1,3-benzothiazol-2-yl[2-(4-methyl-1-piperazinyl)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl[2-(4-morpholinyl)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl[2-(methylanino)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl(2-{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-4-pyrimidinyl)-acetonitrile
- 10 1,3-benzothiazol-2-yl{2-[4-(benzyloxy)-1-piperidinyl]-4-pyrimidinyl} acetonitrile
- 1,3-benzothiazol-2-yl[2-(4-hydroxy-1-piperidinyl)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl(2-{[2-(dimethylamino)ethyl]amino}-4-pyrimidinyl)acetonitrile
- 1,3-benzothiazol-2-yl[2-(dimethylamino)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl{2-[(2-methoxyethyl)amino]-4-pyrimidinyl} acetonitrile
- 15 1,3-benzothiazol-2-yl{2-[(2-hydroxyethyl)amino]-4-pyrimidinyl} acetonitrile
- 1,3-benzothiazol-2-yl[2-(propylamino)-4-pyrimidinyl]acetonitrile
- 1,3-benzothiazol-2-yl(2-{[3-(1H-imidazol-1-yl)propyl]amino}-4-pyrimidinyl)acetonitrile
- 1,3-benzothiazol-2-yl[2-(1-pyrrolidinyl)-4-pyrimidinyl]acetonitrile
- 20 1,3-benzothiazol-2-yl{2-[(2-phenylethyl)amino]-4-pyrimidinyl} acetonitrile

- 1,3-benzothiazol-2-yl(2-{[2-(2-pyridinyl)ethyl]amino}-4-pyrimidinyl)acetonitrile
- 1,3-benzothiazol-2-yl{2-[(2-pyridinylmethyl)amino]-4-pyrimidinyl}acetonitrile
- 1,3-benzothiazol-2-yl{2-[4-(1H-1,2,3-benzotriazol-1-yl)-1-piperidinyl]-4-pyrimidinyl}acetonitrile
- 5 1,3-benzothiazol-2-yl{2-[4-(2-pyrazinyl)-1-piperazinyl]-4-pyrimidinyl}acetonitrile
- 1,3-benzothiazol-2-yl{2-[4-(2-pyrimidinyl)-1-piperazinyl]-4-pyrimidinyl}acetonitrile
- 1,3-benzothiazol-2-yl(2-{[2-(3-pyridinyl)ethyl]amino}-4-pyrimidinyl)acetonitrile
- 1,3-benzothiazol-2-yl(5-bromo-2-{[2-(dimethylamino)ethyl]amino}-4-pyrimidinyl)-acetonitrile
- 10 1,3-benzothiazol-2-yl{2-[(2-morpholin-4-ylethyl)amino]pyrimidin-4-yl}acetonitrile
- 1,3-benzothiazol-2-yl[2-(4-{3-[(trifluoromethyl)sulfonyl]anilino}piperidin-1-yl)pyrimidin-4-yl]acetonitrile
- 1,3-benzothiazol-2-yl(2-{[3-(2-oxopyrrolidin-1-yl)propyl]amino}pyrimidin-4-yl)-acetonitrile
- 15 1,3-benzothiazol-2-yl(2-{methyl[3-(methylamino)propyl]amino}pyrimidin-4-yl)acetonitrile
- 1,3-benzothiazol-2-yl(2-{[3-(4-methylpiperazin-1-yl)propyl]amino}pyrimidin-4-yl)-acetonitrile
- 1,3-benzothiazol-2-yl{2-[(3-morpholin-4-ylpropyl)amino]pyrimidin-4-yl}acetonitrile
- 20 1,3-benzothiazol-2-yl(2-{[2-(1-methyl-1H-imidazol-4-yl)ethyl]amino}pyrimidin-4-yl)acetonitrile
- 1,3-benzothiazol-2-yl(2-{[2-(1H-indol-3-yl)ethyl]amino}pyrimidin-4-yl)acetonitrile

- 1,3-benzothiazol-2-yl(2-{[2-(4-hydroxyphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile
- tert-butyl ({4-[1,3-benzothiazol-2-yl(cyano)methyl]pyrimidin-2-yl} amino)acetate
- {2-[(3-aminopropyl)amino]pyrimidin-4-yl}(1,3-benzothiazol-2-yl)acetonitrile
- {2-[(2-aminoethyl)amino]pyrimidin-4-yl}(1,3-benzothiazol-2-yl)acetonitrile
- 5 1,3-benzothiazol-2-yl(2-{[3-(dimethylamino)propyl]amino}pyrimidin-4-yl)acetonitrile
- 1,3-benzothiazol-2-yl{2-[(2-piperidin-1-ylethyl)amino]pyrimidin-4-yl}acetonitrile
- 1,3-benzothiazol-2-yl(2-{[2-(1-methyl-1H-imidazol-5-yl)ethyl]amino}pyrimidin-4-yl)acetonitrile
- 1,3-benzothiazol-2-yl[2-(benzylamino)pyrimidin-4-yl]acetonitrile
- 10 isopropyl 3-({4-[1,3-benzothiazol-2-yl(cyano)methyl]pyrimidin-2-yl} amino)propanoate
- 1,3-benzothiazol-2-yl{2-[(3-hydroxypropyl)amino]pyrimidin-4-yl}acetonitrile
- 1,3-benzothiazol-2-yl{2-[(pyridin-3-ylmethyl)amino]pyrimidin-4-yl}acetonitrile
- 1,3-benzothiazol-2-yl{2-[(pyridin-4-ylmethyl)amino]pyrimidin-4-yl}acetonitrile
- 15 tert-butyl 4-[2-({4-[1,3-benzothiazol-2-yl(cyano)methyl]pyrimidin-2-yl} amino)-ethyl]phenylcarbamate
- (2-{[2-(4-aminophenyl)ethyl]amino}pyrimidin-4-yl)(1,3-benzothiazol-2-yl)acetonitrile
- 1,3-benzothiazol-2-yl(2-{[2-(3,4-dimethoxyphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile
- 20 1,3-benzothiazol-2-yl(2-{[2-(3-methoxyphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

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1,3-benzothiazol-2-yl(2-{[2-(2-fluorophenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl[2-(2-[3-(trifluoromethyl)phenyl]ethyl)amino]pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl{2-[2-(2-hydroxy-2-phenylethyl)amino]pyrimidin-4-yl}acetonitrile

5 1,3-benzothiazol-2-yl{2-[2-{[3-(trifluoromethyl)pyridin-2-yl]amino}ethyl]amino]-pyrimidin-4-yl}acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(3-chlorophenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(3,4-dichlorophenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

10 1,3-benzothiazol-2-yl(2-{[2-(4-methoxyphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(4-methylphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(3-fluorophenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

15 1,3-benzothiazol-2-yl(2-{[2-(4-phenoxyphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(2-phenoxyphenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(4-bromophenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(4-fluorophenyl)ethyl]amino}pyrimidin-4-yl)acetonitrile

20 1,3-benzothiazol-2-yl{2-[2-[1,1'-biphenyl]-4-ylethyl]amino]pyrimidin-4-yl}acetonitrile

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1,3-benzothiazol-2-yl{2-[(2-{4-[hydroxy(oxido)amino]phenyl}ethyl)amino]pyrimidin-4-yl}acetonitrile

1,3-benzothiazol-2-yl(2-{[2-(1H-1,2,4-triazol-1-yl)ethyl]amino}pyrimidin-4-yl)acetonitrile

5 1,3-benzothiazol-2-yl(2-{[3-(1H-pyrazol-1-yl)propyl]amino}pyrimidin-4-yl)acetonitrile

4-[2-({4-[1,3-benzothiazol-2-yl(cyano)methyl]pyrimidin-2-yl}amino)ethyl]benzene-sulfonamide

10 {2-[(2-pyridin-3-ylethyl)amino]pyrimidin-4-yl}[5-(trifluoromethyl)-1,3-benzothiazol-2-yl]acetonitrile

1,3-benzothiazol-2-yl{2-[(1H-tetraazol-5-ylmethyl)amino]pyrimidin-4-yl}acetonitrile

1,3-benzothiazol-2-yl[2-(benzyloxy)pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl{2-[(4-pyridin-3-ylbenzyl)oxy]pyrimidin-4-yl}acetonitrile

1,3-benzothiazol-2-yl[2-(pyridin-4-ylmethoxy)pyrimidin-4-yl]acetonitrile

15 1,3-benzothiazol-2-yl[2-(pyridin-2-ylmethoxy)pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl[2-(3-pyridin-2-ylpropoxy)pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl{2-[(4-methoxybenzyl)oxy]pyrimidin-4-yl}acetonitrile

1,3-benzothiazol-2-yl[2-(pyridin-3-ylmethoxy)pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl{2-[2-(4-methoxyphenyl)ethoxy]pyrimidin-4-yl}acetonitrile

20 1,3-benzothiazol-2-yl[2-([1,1'-biphenyl]-3-ylmethoxy)pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl{2-[(3,4,5-trimethoxybenzyl)oxy]pyrimidin-4-yl}acetonitrile

- 1,3-benzothiazol-2-yl{2-[(3,4-dichlorobenzyl)oxy]pyrimidin-4-yl}acetonitrile
- 1,3-benzothiazol-2-yl[2-(3-[(dimethylamino)methyl]benzyl)oxy]pyrimidin-4-yl]acetonitrile
- 1,3-benzothiazol-2-yl{2-[(1-oxidopyridin-3-yl)methoxy]pyrimidin-4-yl}acetonitrile
- 5 1,3-benzothiazol-2-yl(2-{[4-(morpholin-4-ylmethyl)benzyl]oxy}pyrimidin-4-yl)acetonitrile
- 1,3-benzothiazol-2-yl{2-[(4-pyridin-2-ylbenzyl)oxy]pyrimidin-4-yl}acetonitrile
- 1,3-benzothiazol-2-yl(2-{[4-(piperidin-1-ylmethyl)benzyl]oxy}pyrimidin-4-yl)acetonitrile
- 10 1,3-benzothiazol-2-yl[2-(4-methoxyphenoxy)pyrimidin-4-yl]acetonitrile
- 1,3-benzothiazol-2-yl[2-(4-butoxyphenoxy)pyrimidin-4-yl]acetonitrile
- {2-[4-(4-acetyl)piperazin-1-yl]phenoxy]pyrimidin-4-yl}(1,3-benzothiazol-2-yl)acetonitrile
- [2-(4-methoxyphenoxy)pyrimidin-4-yl][5-(trifluoromethyl)-1,3-benzothiazol-2-yl]acetonitrile
- 15 N-[2-(4-[1,3-benzothiazol-2-yl(cyano)methyl]pyrimidin-2-yl)amino)ethyl]-4-chlorobenzamide
- 1,3-benzothiazol-2-yl(2-methoxy-4-pyrimidinyl)acetonitrile
- 1,3-benzothiazol-2-yl[2-(4-{[4-(4-methylpiperazin-1-yl)methyl]benzyl}oxy)pyrimidin-4-yl]acetonitrile
- 20 1,3-benzothiazol-2-yl[2-(4-{[4-(4-benzyl-piperazin-1-yl)methyl]benzyl}oxy)pyrimidin-4-yl]acetonitrile

1,3-benzothiazol-2-yl(2-{[4-(piperazin-1-ylmethyl)benzyl]oxy}pyrimidin-4-yl)acetonitrile

1,3-benzothiazol-2-yl[2-(4-{[4-(4-formylpiperazin-1-yl)methyl]benzyl}oxy)pyrimidin-4-yl]acetonitrile

5 [2-(4-{[4-(4-acetylpiperazin-1-yl)methyl]benzyl}oxy)pyrimidin-4-yl](1,3-benzothiazol-2-yl)acetonitrile

(3H-Benzothiazol-2-ylidene)-{2-[4-(4-[1,2,4]oxadiazol-3-ylmethyl-piperazin-1-ylmethyl)-benzyloxy]-pyrimidin-4-yl}-acetonitrile

10 4-(4-{4-[(3H-Benzothiazol-2-ylidene)-cyano-methyl]-pyrimidin-2-yloxymethyl}-benzyl)-piperazine-1-carboxylic acid methyl ester

2-[4-(4-{4-[(3H-Benzothiazol-2-ylidene)-cyano-methyl]-pyrimidin-2-yloxymethyl}-benzyl)-piperazin-1-yl]-acetamide

(2-{4-[4-(2-Amino-acetyl)-piperazin-1-ylmethyl]-benzyloxy}-pyrimidin-4-yl)-(3H-benzothiazol-2-ylidene)-acetonitrile

15 [4-(4-{4-[(3H-Benzothiazol-2-ylidene)-cyano-methyl]-pyrimidin-2-yloxymethyl}-benzyl)-piperazin-1-yl]-acetic acid methyl ester

(3H-Benzothiazol-2-ylidene)-(2-{4-[4-(2-methoxy-ethyl)-piperazin-1-ylmethyl]-benzyloxy}-pyrimidin-4-yl)-acetonitrile

20 4-(4-{4-[(3H-Benzothiazol-2-ylidene)-cyano-methyl]-pyrimidin-2-yloxymethyl}-benzyl)-piperazine-1-carboxylic acid dimethylamide

(3H-Benzothiazol-2-ylidene)-{2-[4-(4-ethyl-piperazin-1-ylmethyl)-benzyloxy]-pyrimidin-4-yl}-acetonitrile

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(3H-Benzothiazol-2-ylidene)-(2-{4-[4-(2-hydroxy-ethyl)-piperazin-1-ylmethyl]-benzyloxy}-pyrimidin-4-yl)-acetonitrile

9. Use according to any of the preceding claims further comprising at least one
5 supplementary drug selected from the group consisting of insulin, aldose reductase inhibitors, alpha-glucosidase inhibitors, sulfonyl urea agents, biguanides, thiazolidines, PPARs agonists, GSK-3 inhibitors.
10. Use according to claim 9 wherein said supplementary drug is selected from the group
10 consisting of a rapid acting insulin, an intermediate acting insulin, a long acting insulin, a combination of intermediate and rapid acting insulins, Minalrestat, Tolrestat, Sorbinil, Methosorbinil, Zopolrestat, Epalrestat, Zenarestat, Imirestat, Ponalrestat, ONO-2235, GP-1447, CT-112, BAL-ARI 8, AD-5467, ZD5522, M-16209, NZ-314, M-79175, SPR-210, ADN 138, or SNK-860, Miglitol, Acarbose, Glipizide, Glyburide, Chlorpropamide, Tolbutamide, Tolazamide, or Glimepiride.

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